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Bioresorbable Polylactide Interbody Implants in an Ovine Anterior Cervical Discectomy and Fusion Model: Three-Year Results

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Abstract

Study Design. *In vivo* study of anterior discectomy and fusion using a bioresorbable 70:30 poly(l-lactide-co-d,l-lactide) interbody implant in an ovine model.

Objective. To evaluate the efficacy of the polylactide implant to function as an interbody fusion device, and to assess the tissue reaction to the material during the resorption process.

Summary of Background Data. The use of polylactide as a cervical interbody implant has several potential advantages when compared with traditional materials. Having an elastic modulus very similar to bone minimizes the potential for stress shielding, and as the material resorbs additional loading is transferred to the developing fusion mass. Although preclinical and clinical studies have demonstrated the suitability of polylactide implants for lumbar interbody fusion, detailed information on cervical anterior cervical discectomy and fusion (ACDF) with polylactide devices is desirable.

Methods. Single level ACDF was performed in 8 skeletally mature ewes. Bioresorbable 70:30 poly (l-lactide-co-d,l-lactide) interbody implants packed with autograft were used with single-level metallic plates. Radiographs were made every 3 months up to 1 year, and yearly thereafter. The animals were killed at 6 months (3 animals), 12 months (3 animals), and 36 months (2 animals). In addition to the serial plain radiographs, the specimens were evaluated by nondestructive biomechanical testing and undecalcified histologic analysis.

Results. The bioresorbable polylactide implants were effective in achieving interbody fusion. The 6-month animals appeared fused radiographically and biomechanically, whereas histologic sections demonstrated partial fusion (in 3 of 3 animals). Radiographic fusion was confirmed histologically and biomechanically at 12 months (3 of 3 animals) and 36 months (2 of 2 animals). A mild chronic inflammatory response to the resorbing polylactide implant was observed at both 6 months and 12 months. At 36 months, the operative levels were solidly fused and the implants were completely resorbed. No adverse tissue response was observed in any animal at any time period.

Conclusion. Interbody fusion was achieved using bioresorbable polylactide implants, with no evidence of implant collapse, extrusion, or adverse tissue response to the material. The use of polylactide as a cervical interbody device appears both safe and effective based on these ACDF animal model results.

Among the management options for degenerative or traumatic conditions of the cervical spine, anterior cervical discectomy and fusion (ACDF) continues to be the most popular. The inherent advantages of the anterior approach include its direct muscle sparing approach leading to an unencumbered visualization of the spinal cord and exiting nerve roots, the benefit of complete removal of the degenerative or traumatized intervertebral disc, and the presence of 2 endplates with substantial surface area to yield high fusion rates. Single level ACDF has consistently yielded high fusion rates along with a high rate of clinical success in the amelioration of symptoms referable to nerve root or spinal cord compression. The major debate remaining centers on the use of allograft *versus* autograft.[1-3](#)

Autologous graft, harvested from either the iliac crest bone or fibula, has demonstrated low nonunion rates, but the complications associated with these procedures have all but eliminated their popularity. The principal complications include infection, hematoma, lateral femoral cutaneous nerve palsy, and chronic pain.[4](#) Conversely, the use of allograft raises issues, such as the potential for disease transmission, increased cost and nonunion.

Intervertebral cages have emerged as an alternative to bone graft with the stated advantages of negligible incidence of collapse (leading to kyphosis) and pseudarthrosis.[5](#) The composition of these cages has been the focus of a significant body of research. Metals such as titanium and stainless steel are common implant materials but obscure subsequent radiologic studies, particularly at the developing fusion site. Other biomaterials such as hydroxylapatite and other calcium phosphate ceramics are subject to fracture, collapse, and extrusion.[6](#)

To address these issues, interbody implants made from bioresorbable materials have been studied as an alternative to structural bone grafts or metallic implants to facilitate fusion. Generally the limitations of the use of bioresorbable materials are because of the relatively lower initial strength and the decrease in strength during the polymer degradation process (which begins immediately after implantation), and whether the implant will provide sufficient strength or stability for the intended application. Conversely, bioresorbable polymers have the advantage of radiolucency facilitating greater detail on radiologic imaging without the scatter effect metallic components have on computed tomography (CT) and magnetic resonance imaging. Stress shielding associated with metallic implants is lessened because the material's elastic modulus is close to that of bone, and because there is a gradual increasing transfer of the load across the fusion site as the implant is resorbed. For example, van Dijk *et al* demonstrated a significantly higher rate of fusion using stand alone cages made of poly(l-lactide) when compared with titanium.[7,8](#)

In addition for a bioresorbable implant, there must be minimal reaction to the degradation products to minimize the possibility of an adverse tissue response (for example a foreign body or osteoclastic resorption response). When compared with other bioresorbable materials, such as those consisting of only l-lactide or copolymers containing glycolide, poly(l-lactide-co-d,l-lactide) has been reported to elicit much less of a tissue reaction.[9-13](#) Numerous review articles are available in the literature describing the chemical, physical, and mechanical properties of these materials, as well as the mechanisms of degradation and the body's reaction to the materials and the breakdown products.[14-19](#) Recently, reviews have summarized specifically the preclinical and clinical literature demonstrating the potential of bioresorbable materials as interbody implants.[20-24](#)

In the present study, we evaluated the safety and efficacy of cervical interbody implant made from high molecular weight, amorphous 70:30 poly(l-lactide-co-d,l-lactide) in an ovine ACDF model.

Materials and Methods

Implants

The bioresorbable interbody implants were fabricated by MacroPore Biosurgery (San Diego, CA) from commercially available 70:30 poly(l-lactide-co-d,l-lactide), or PLDLLa, raw material (Boehringer-Ingelheim, Ingelheim, Germany). The raw material consists of a random arrangement of 70% l-lactide, and 30% d,l-lactide; within the 30% d,l-lactide, there is 50% l-lactide and 50% d-lactide, also in a random arrangement. Thus the material is a random arrangement of 85% l-lactide and 15% d-lactide. The specifications for the raw material included an inherent viscosity of 5.5 to 6.5 dL/g, and residual monomer less than 0.5%. The raw material molecular weight (M_w , weight average) was approximately 950,000 to 1,000,000 g/mol. As manufactured, this 70:30 PLDLLa material has been shown to retain up to 100% of its initial compressive strength after 26 weeks,²⁵ or longer depending on the implant design, indicating its potential for interbody applications. *In vitro* ageing of devices of the same design as in the present study (but with 10 mm height and a 2.5 mm wall thickness) withstood an initial maximum compressive load of 5633 N and maintained 99% of this compressive strength to 52 weeks (unpublished data, MacroPore Biosurgery). Polymer analysis also demonstrated the material was amorphous (no crystallinity) in various fabricated forms for up to 52 weeks or longer.^{26,27}

All implants were fabricated, packaged, and sterilized using qualified processes identical to those used for manufacturing of commercial implants from the 70:30 PLDLLa raw material. The implants were fabricated by injection molding, followed by machining of features into the final implant shape. The implants measured 11 x 11 x 7 mm (width x length x height), with a central open region (hole) and a 2 mm wall thickness. The device had flat endplates with parallel notches to limit migration, slightly converging lateral sides, and a curved anterior (ventral) aspect. Tantalum markers (0.5 mm O) were inserted into each device, 1 anteriorly and 2 posteriorly, to allow radiographic monitoring of the radiolucent implant. The bioresorbable interbody implant is shown in [Figure 1](#). All samples were placed in standard packaging and sterilized by electron beam (e-beam) by a commercial medical device sterilization vendor using a standard, qualified process.

In this animal study the bioresorbable interbody implants were used in conjunction with single level metallic plates and screws. Because of the anatomy and posture of the animals, and the impossibility of restricting movement of the cervical spine, the plates prevented early extrusion of the interbody implant. The use of plates in this model is similar to common clinical practice for patients who desire an earlier return to activities of daily living or the workplace, who may have comorbidities that may affect their ability to fuse, or who may be noncompliant regarding the use of an orthosis.

Surgical Procedures

Under an IACUC approved protocol, 8 skeletally mature Rambouillet x Columbian ewes were anesthetized using diazepam (0.1 mg/kg, IV) and ketamine (3.3 mg/kg) for induction, and isoflurane inhalation (1.5%-4% in 100% oxygen at 2 L/min) for maintenance. Under anesthesia in dorsal recumbency, the ventral (anterior) cervical spine and sternum were clipped and prepared and draped for sterile surgery in a routine manner using alternating scrubs of povidone iodine and alcohol. An 8-cm incision was made over the sternum. After partial reflection of the skin and subcutaneous tissues, an osteotome was used to create a small window in the ventral cortex of the

sternum. Using a curette, approximately 2 cm³ of autogenous cancellous bone was removed. The sternal incision site was closed using resorbable subcutaneous suture and stainless steel skin staples.

Ventral (anterior) exposure and discectomy was then performed. A midline ventral (anterior) incision was made from the thyroid cartilage to the manubrium sternum. The paired sternohyoid and sternomastoid muscles were separated on their midline. The esophagus and trachea and the carotid sheaths were digitally retracted. At the selected disc space vertebral spreaders were applied, the longus coli muscles were elevated, subperiosteally, followed by discectomy. In 4 animals the C3-C4 level was used, C4-C5 was used in 3 animals, and C5-C6 was used in 1 animal. The interior of the bioresorbable interbody implant was packed with cancellous autograft harvested from the sternum. Under distraction the endplates were removed down to bleeding bone, as parallel as possible, using a high-speed burr and the device implanted. To prevent anterior migration of the device, single-level F136 titanium alloy plates and screws were used (Atlantis Plates, Medtronic Sofamor Danek, Memphis, TN). The plates were 24 mm in length, and the screws were 4 mm O, 12 mm in length (4 per animal). After plating, routine closure of the longus coli muscle (size 0 absorbable suture), subcutaneous tissues (size 2-0 absorbable suture), and the skin (size 2-0 nonabsorbable monofilament suture) were performed.

All animals received phenylbutazone (1 g, orally) 1 day before surgery, on the day of surgery, and for 3 days after surgery. All animals also received fentanyl (150 [mu]g/h) by transdermal patches beginning 1 day before surgery through the second postoperative day. Prophylactic antibiotics were given perioperatively (cefazolin sodium, 1 g, iv). After surgery, all animals were monitored continually for pain for 4 to 6 hours, and then received standard postoperative treatment and care. Dorsoventral (anteroposterior) and lateral radiographs were taken immediately after surgery and every 3 months for the first 12 months, and then every 12 months until sacrifice.

Animals were randomly selected for termination at 6, 12, or 36 months after surgery. Euthanasia was achieved by pentobarbital sodium overdose, the cervical spine was harvested *en bloc*, including at least an additional level above and below the surgical site, and immediately frozen and forwarded for biomechanical testing.

Biomechanical Testing

Before testing, the specimens were thawed and cleaned of muscle tissues without damaging the ligaments, discs, or joint capsules. The metallic plates and screws were not removed before testing. Wood screws were partially inserted into the facet articulations and endplates, and the screw heads embedded in polymethylmethacrylate within cylindrical fixtures for application of the test loads.

Nonconstraining, nondestructive pure moment (torque) loading was applied to each specimen as previously described.[28,29](#) Torque loading was applied through a system of cables and pulleys in conjunction with a standard servo-hydraulic test system (MTS Systems, Minneapolis MN). Loading was applied to induce flexion, extension, left and right lateral bending, and left and right axial rotation. Three preconditioning cycles were first applied in each loading mode by ramping to 5.0 Nm and holding for 60 seconds before releasing. After preconditioning, the specimens rested for 60 seconds, followed by loading to a maximum of 5.0 Nm, applied in increments of 1.0 Nm of 45 seconds each. Maximum loads of 5.0 Nm were used because it was expected that this magnitude would more effectively demonstrate differences between fused and unfused segments than smaller loads sometimes used for cervical flexibility testing. Loads of 5.0 Nm are similar to those used by other researchers studying ovine cervical biomechanics.[30-32](#) Motion at the operated level and the adjacent cranial and caudal levels in response to the applied loading was measured in three-

dimensions using the Optotrak 3020 system (Northern Digital, Waterloo, Ontario, Canada). The Optotrak system measured the 3-dimensional displacement of infrared light emitting markers rigidly fixed to each vertebra. Custom software converted the marker displacement coordinates to angles with respect to the anatomic axes at the index and adjacent levels.[33,34](#) After the biomechanical testing, the specimens were fixed in buffered formalin and forwarded for undecalcified histologic and microradiographic evaluation.

Histologic Evaluation

High-resolution radiographs of the harvested spines were made using a high-resolution system (Faxitron, Hewlett Packard, McMinnville, OR; Ektascan B/RA 4153 film, Eastman-Kodak, Rochester, NY). PA and lateral radiographs were made before and after removal of the metallic plates and graded to assess fusion; these radiographs were also used for orientation to prepare the samples for histologic analysis as described below. The Faxitron radiographs were graded as follows: 1 = nonfusion; 2 = lucency with some bony bridging; 3 = increased bone density; 4 = continuous bony bridging. On the lateral radiographs, the center of the disc space as well as the anterior and posterior margins were evaluated; on the PA radiographs, the center of the disc space as well as the medial and lateral margins were evaluated. An overall fusion score for the spinal level was determined: Grade 1 was a nonfusion with significant radiolucent lines in the through-growth region of the implant; Grade 2 was a probable fusion with some radiolucent lines in the through-growth region of the implant; and Grade 3 was a solid interbody fusion with no radiolucent lines in the through-growth region of the implant.

After radiography, all spinal levels containing an implant were sectioned in the sagittal plane to produce 2 sagittal slabs and processed by undecalcified histology. Both slabs from each animal were sequentially dehydrated in alcohol, cleared in a clearing agent, and embedded in graded catalyzed methyl methacrylate. After polymerization was complete and the samples were hardened, the blocks containing explants and surrounding tissues were sectioned on diamond saws (Buehler Isomet, Lake Bluff, IL) to an approximate thickness of 150 to 400 μm . Approximately 18 sections (total per spinal level) were made in the sagittal plane through the explant blocks. If necessary, grinding was performed to obtain the desired thickness. Differential staining using a proprietary multiple stain was used to permit differentiation of bone, cartilage, fibrocartilage, and fibrovascular tissues. Staining of cellular and nuclear detail by the trichrome stain (similar to H&E) permitted cytologic differentiation.

Approximately 8 undecalcified sections from each spinal level were selected for microradiography. These sections were radiographed using a Faxitron radiography unit (Hewlett Packard, McMinnville, OR) and spectroscopic film (EM-1 film, Kodak, Rochester, NY). Sections were exposed to the radiograph source at 20 kV and 3 mA for approximately 45 seconds for each 100 μm of section thickness.

Individual undecalcified sections were evaluated for fusion in the anterior margin, in the middle (through-growth) region of the polylactide implant, and in the posterior margin. These anatomic locations for each section were considered to be fused only if continuous bony bridging was found from superior to inferior. Based on all sections evaluated from each spine, the spinal level was considered to be fused if greater than 50% of the sections showed continuous bony bridging in any of the 3 anatomic regions; a partial fusion existed if less than 50% of the sections showed continuous bony bridging in any of the 3 anatomic regions, and a nonfusion existed if none of the sections showed continuous bony bridging.

To characterize the host response to the polymer implant material, and polymer degradation products (if present), sections were scored using ASTM F981.³⁵ This standard was used to evaluate necrosis, degeneration, inflammation, fibrosis, foreign body debris, fatty infiltration, and the presence of giant cells/osteoclasts. While ASTM F981 does not include osteoclasts, this modification was used because the differentiation of giant cells from osteoclasts is not always possible in osseous tissues.

Results

There were no surgical or postoperative complications observed in any animal. Animals were killed at 6 and 12 months (3 animals each), and at 36 months (2 animals).

A total of 28 sets of plain radiographs were evaluated from 3, 6, 9, 12, 24, and 36 month follow-up time points. In 2 animals (killed at 36 months), the 6-month follow-up radiographs were not available. Screw back-out occurred in 2 animals at 6 months after surgery (1 screw in each) and each progressed without complications thereafter (each was killed at 36 months). Radiographic evidence of a developing fusion was present at 3 months and confirmed at all time periods thereafter. There was no evidence of any significant loss of disc space (height) as the fusion developed, nor was there evidence of any adverse tissue reaction to the resorbing polymer material or any evidence of osteolysis. In no radiograph from any animal was there any evidence of movement of the implant, nor was there migration of any of the tantalum markers.

Biomechanical Testing

The results of the biomechanical testing are summarized for all animals in [Table 1](#). As expected, there was a marked decrease in the range of motion in all loading modes at the fusion level as compared to the adjacent levels. The biomechanical testing indicated fusion at the 6-month time period, with less than 0.5[degrees] ROM at the fusion level in each loading mode. The largest ROM observed was in lateral bending, followed by extension, both at the adjacent caudal levels. The motion observed in all loading modes showed no consistent change over time from 6 to 36 months. At the fusion level, the average ROM for all modes at all time periods was 0.23[degrees] (range, 0.06-0.40[degrees]). For all adjacent (unfused) levels, the average ROM for all modes at all time periods was 11.19[degrees] (range, 3.10-21.40[degrees]). The individual ROM results for each animal are shown in [Figure 2](#).

Radiographic Evaluation of Fusion

Radiographic evaluation of fusion, based on the postsacrifice Faxitron radiographs, was performed by 2 independent evaluators blinded to survival time. For the 6 month animals, one was rated as a solid fusion by both evaluators, whereas the remaining 2 animals each were rated as a probable fusion by one evaluator and as a solid fusion by the other evaluator. All three 12-months animals were rated as solid fusions by both evaluators, as were the two 36-month animals.

Histologic Evaluation

Using the criteria described for evaluating the sections, there were no histologic nonfusions at any time period. At 6 months, all 3 of the treated levels generated partial histologic fusions, often limited to the anterior margins on the medial or lateral side of the levels. The 6 month, stained undecalcified sections and corresponding microradiographs through the center of the disc space

(through center of implant) did not show continuous bony bridging from superior to inferior ([Figure 3](#)). The polylactide devices were intact, with evidence of fissures in the sections, and surrounded by quiescent fibrous tissue. All animals at 6 months were graded as having a mild chronic inflammatory response (score of 1.0, per ASTM F981).

At 12 months, all treated levels (3 animals) showed a histologic fusion with continuous bony bridging within the polylactide device ([Figure 4](#)). In contrast to the 6-month time period, the polylactide implants exhibited visible resorption of features such as the peaks of the serrations (teeth) and corners of the device. At 1 year, some polylactide device fragments were present in peri-implant tissues. Quiescent fibrous tissues of varying thickness and resembling a capsule were present at the polylactide device interface. Interdigitations along the endplate surfaces of the polylactide implant were filled with bone but separated from the polylactide implant by a thin layer of fibrous tissue. As observed at 6 months, the tissue response of all animals was graded as mild chronic inflammation (score of 1.0, per ASTM F981).

Discussion

The comparison of results from preclinical studies is often problematic because of differences in the study design, implant materials, methodologies and endpoints used. With respect to bioresorbable materials, sufficient details are needed to completely describe the material used, including the raw material and the processing used to manufacture the implant studied, to insure that valid comparisons can be made as described below. The description of materials in general terms (*e.g.*, polylactide) rather than specifically (*e.g.*, 70:30 poly(l-lactide-co-d,l-lactide)) may at best lead to confusion, and at worst the idea that all bioresorbable materials are alike.

The results of the present study, in terms of the development of fusion, were consistent with previous preclinical and short-term clinical studies of the same material (identically manufactured 70:30 PLDLLa).[36-39](#) Toth *et al* reported on a threaded lumbar interbody device with autograft or rhBMP2 in an ovine model.[36](#) The mean radiographic scores indicated probable fusion for all animals at 6 and 12 months, and solid fusion at 18 months. Histologic sections showed half of the 6 months animals to be fused (1 of 2 animals in each group), and at 12 months 3 of 4 autograft animals and 1 of 2 rhBMP2 animals were solid fusions. All animals at 18 and 24 months demonstrated solid histologic fusion, although analysis was not complete on all 24 months animals. The tissue response was graded as a mild to moderate inflammatory response at all time periods, with no osteolysis or adverse response to the degradation products of the polymer. At 24 months significant, though incomplete, resorption of the interbody device had occurred. The larger implant design and greater volume of PLDLLa used in the study by Toth *et al* may explain the slight difference in tissue response and the remaining polymer at 24 months; the influence cage design has been summarized by Wuisman and Smit.[23](#)

The results of the present study are in sharp contrast to the findings reported by Kandziora *et al*.[40](#) They reported on ACDF with plating in a sheep model using tricortical iliac crest autograft, 70:30 poly(l-lactide-co-d,l-lactide) cages, and a polymer-calcium phosphate composite cage (8 animals in each group). All animals were killed at 12 weeks after surgery, and the 70:30 poly(l-lactide-co-d,l-lactide) cages were reported to be equivalent to the iliac crest autograft. However, they reported all of the 70:30 poly(l-lactide-co-d,l-lactide) cages to have mild (<1 mm) to severe (>3 mm) osteolysis around the implant. In the present study, there was no suggestion of osteolysis on any postoperative radiograph, nor in any histologic section in any animal at 6, 12, or 36 months; the tissue reaction to the 70:30 PLDLLa implant and the degradation products elicited at worst a mild

inflammatory response which was completely absent at 36 months. Wuisman *et al*⁴¹ have commented on several aspects of the work by Kandziora *et al*, particularly the inadequate details of the material used and whether the findings Kandziora reported are comparable to other preclinical and clinical studies of 70:30 PLDLLa.

Clinical reports of 70:30 PLDLLa used as interbody implants in cervical ACDF are limited to retrospective series with relatively short-term follow-up,³⁷⁻³⁹ with no randomized, prospective series published to date. These limited results, however, have demonstrated good to excellent clinical results with a commercial implant very similar to those used in the present animal study (commercial device has various heights, a 2.5-mm wall thickness, and no tantalum markers; Cornerstone HSR implant, manufactured by MacroPore Biosurgery for Medtronic Sofamor Danek, Memphis, TN). Vaccaro *et al*³⁷ reported on 8 patients who had single or multilevel ACDF with plating having good (3) to excellent (5) results by Odom's criteria, although the follow-up period was only 6 to 7 months. At that follow-up time point, 17 of 18 levels were graded as radiographically fused. A group of 20 patients who received the same implant augmented with rhBMP2 were studied by Lanman and Hopkins.³⁸ This cohort included ACDF with plating at a single level in 14 patients, 2 levels in 4 patients, and 3 levels in 2 patients (total of 28 levels). Fusion was assessed by CT scan and defined as bone bridging in the interbody space through the bioresorbable implant. All levels were fused at both 3 months (28 of 28 levels in 20 patients), and at 6 months (24 of 24 levels in 17 patients). This series was later reported at a minimum follow-up period of 12 months (range, 12-18 months) with the cohort including 27 patients. All patients were fused at 3 months, and at a minimum of 12 months (by CT scan) in 42 of 42 operated levels, with no implant related complications.³⁹

In evaluating the biomechanical stability of the explanted spine segments, the metallic plates were left in place. Dissecting and removing the plates would have been infeasible because of the large overgrowth of the fusion mass and would likely have damaged the fusion mass, confounding the results. Therefore, the stability observed may have exceeded the stability of the fusion mass if it had been evaluated independently. However, it was shown previously that the ROM across incompletely fused plated ovine cervical motion segments with interbody spacers far exceeds the values observed in the present study, with mean ROM as high as 3.4[degrees] under 6 Nm load.⁴⁰ Therefore the small ROM observed in the present study most likely represent fusion.

The limitations of the present study include the numbers of animals used and the time points chosen for evaluation of the histologic endpoints. Ideally additional animals and time points would have been desirable, with perhaps a control group of metallic or nonresorbable interbody implants, or a control group with structural autograft. Additional time points between 6 and 12 months would have clarified the duration of the mild inflammatory response observed. To determine more precisely the time required for complete resorption to occur, time points between 12 and 36 months would have been desirable. Finally the use of metallic plates, while not a limitation *per se*, is generally required by animal care and use committees, because of the high rate of early complications and euthanasia in nonplated ACDF, and could introduce a confounding variable.

In summary, the use of 70:30 PLDLLa as an interbody spacer resulted in partial histologic fusion at 6 months and solid bony fusion at 12 and 36 months. The nondestructive biomechanical testing ROM data suggested all animals were fused with no ROM greater than 0.5[degrees] at the operative level. Because of the time points studied, it is not possible to know exactly when bony fusion occurred. Plain radiographs were predictive of bony fusion at 6 months, and correlated with histologic results for fusion thereafter. This suggests that other imaging methods may be useful in the early postoperative period, even with a radiolucent implant, in patients with concern regarding the status

of their fusion. Although not a specific goal of this study, the finding of no migration of any of the tantalum markers suggests that the radiopaque markers were stable within the device even during resorption. This may suggest that the risk is low of late complications due to marker migration to an undesirable location, or of a "false positive" implant complication. Resorption of the 70:30 PLDLLa implant was associated with a mild chronic inflammatory response until 12 months, or longer, with complete resorption and no associated tissue response occurring between 12 and 36 months. In no animal at any time period was there any evidence of an adverse tissue reaction or osteolysis.

Key Points

* Histology demonstrated partial fusion at 6 months and complete fusion at 12 and 36 months, although all animals had radiographic evidence of fusion after 6 months.

* Nondestructive biomechanical testing results were consistent with the partial or complete histologic fusion, with no ROM greater than 0.5[degrees] at the operative level in any loading mode.

* No adverse tissue response was observed in any animal. A mild chronic inflammatory response to the degrading polylactide implants was observed at 6 and 12 months, whereas at 36 months there was no tissue reaction and the polylactide was completely resorbed.

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Key words: bioresorbable interbody implant; polylactide; 70:30 poly(l-lactide-co-d,l-lactide); PLDLLA; ACDF; animal model

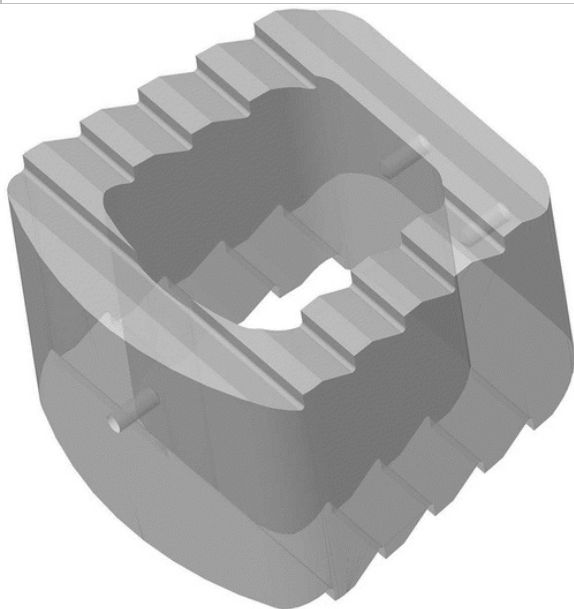


Figure 1. Bioresorbable interbody implant fabricated from 70:30 poly(l-lactide-co-d,l-lactide) raw material. The implants measured 11 x 11 x 7 mm (width x length x height), with a 2-mm wall

thickness. To allow radiographic monitoring of the radiolucent implant 0.5 mm O tantalum markers were inserted into each device (1 anteriorly and 2 posteriorly).

Table 1. Mean Angular Range of Motion (Degrees) at Operative Level, and Adjacent Cranial and Caudal Levels

	Flexion			Extension			Lateral Bending			Axial Rotation		
	Cranial Level	Fusion Level	Caudal Level	Cranial Level	Fusion Level	Caudal Level	Cranial Level	Fusion Level	Caudal Level	Cranial Level	Fusion Level	Caudal Level
6 mo (n = 3 animals)												
Max	13.18	0.35	15.71	14.69	0.30	16.56	18.71	0.40	15.70	8.16	0.26	15.87
Min	5.48	0.18	8.53	6.39	0.13	10.06	14.07	0.11	14.27	3.10	0.18	7.56
Avg	8.44	0.24	11.84	9.68	0.23	13.22	15.93	0.27	15.03	6.09	0.22	11.46
12 mo (n = 3 animals)												
Max	7.84	0.34	12.82	9.95	0.20	16.03	15.97	0.35	18.83	6.86	0.22	7.50
Min	4.66	0.22	7.58	5.65	0.14	9.02	13.30	0.23	14.91	3.41	0.21	5.40
Avg	6.02	0.30	10.09	7.41	0.16	12.22	14.36	0.27	17.46	4.79	0.21	6.41
36 mo (n = 2 animals)												
Max	8.64	0.40	14.92	10.46	0.38	21.40	14.48	0.24	21.38	6.34	0.29	14.80
Min	6.84	0.09	13.45	9.32	0.09	15.13	14.47	0.06	15.94	4.70	0.10	3.76
Avg	7.74	0.25	14.18	9.89	0.23	18.27	14.48	0.15	18.66	5.52	0.20	9.28

Table 1. Mean Angular Range of Motion (Degrees) at Operative Level, and Adjacent Cranial and Caudal Levels

Flexion Extension Lateral Bending Axial Rotation

	Crani al Level	Fusio n Level	Caud al Level		Crani al Level	Fusio n Level	Caud al Level		Crani al Level	Fusio n Level	Caud al Level		Crani al Level	Fusio n Level	Caud al Level
6 mo (n = 3 animals)															
Max	13.18	0.35	15.71		14.69	0.30	16.56		18.71	0.40	15.70		8.16	0.26	15.87
Min	5.48	0.18	8.53		6.39	0.13	10.06		14.07	0.11	14.27		3.10	0.18	7.56
Avg	8.44	0.24	11.84		9.68	0.23	13.22		15.93	0.27	15.03		6.09	0.22	11.46
12 mo (n = 3 animals)															
Max	7.84	0.34	12.82		9.95	0.20	16.03		15.97	0.35	18.83		6.86	0.22	7.50
Min	4.66	0.22	7.58		5.65	0.14	9.02		13.30	0.23	14.91		3.41	0.21	5.40
Avg	6.02	0.30	10.09		7.41	0.16	12.22		14.36	0.27	17.46		4.79	0.21	6.41
36 mo (n = 2 animals)															
Max	8.64	0.40	14.92		10.46	0.38	21.40		14.48	0.24	21.38		6.34	0.29	14.80
Min	6.84	0.09	13.45		9.32	0.09	15.13		14.47	0.06	15.94		4.70	0.10	3.76
Avg	7.74	0.25	14.18		9.89	0.23	18.27		14.48	0.15	18.66		5.52	0.20	9.28

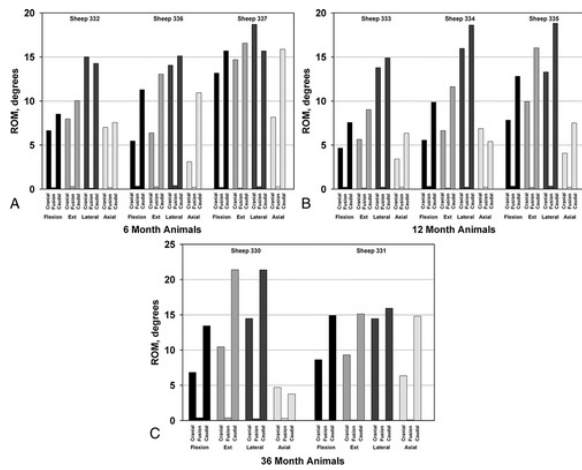


Figure 2. Range of motion (ROM) results for each animal in flexion, extension, lateral bending, and axial rotation. Data are shown at the operative (fusion) level and at the adjacent cranial and caudal (unfused) levels. The maximum ROM observed in any loading mode at the operative level was less than 0.5[degrees]. (A) 6 month results; (B) 12 month results; (C) 36 month results.

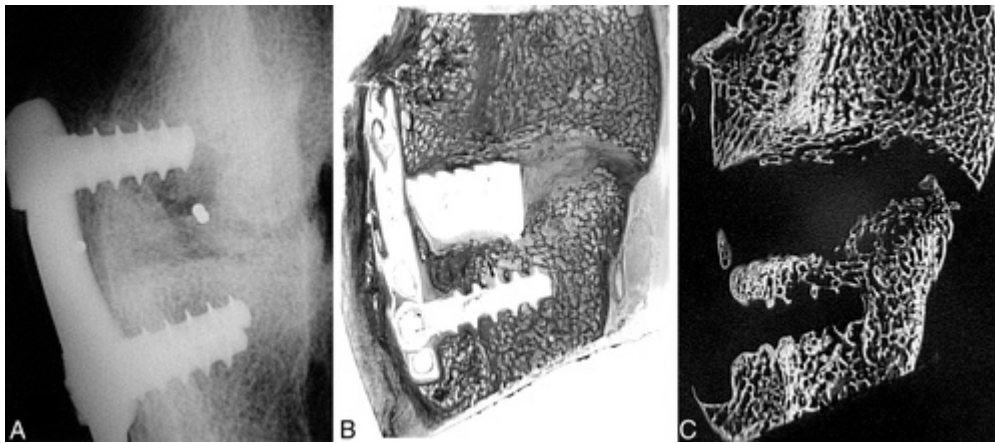


Figure 3. Histologic results at 6 months: (A) postsacrifice high-resolution lateral radiograph; (B) and (C) saggital undecalcified histologic section and corresponding microradiograph. Animal was graded as radiographically fused, and histologic evaluation demonstrated partial fusion. This histologic section shows no bony bridging.

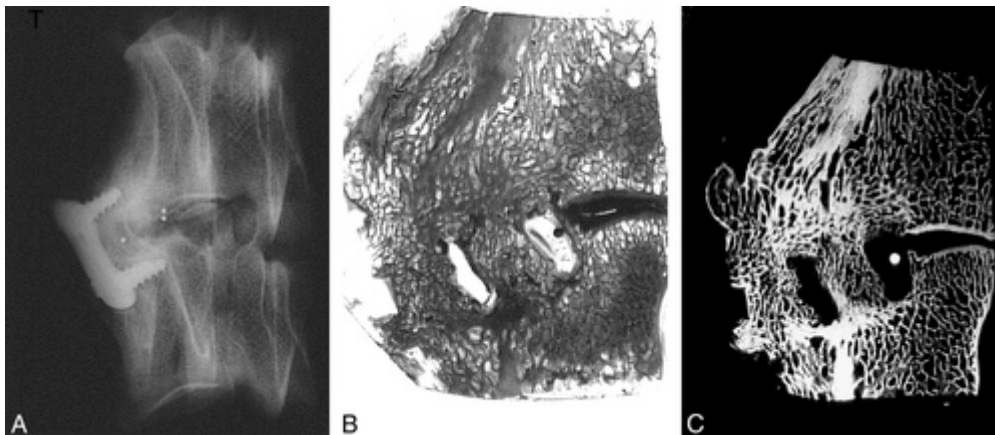


Figure 4. Histologic results at 12 months: (A) postsacrifice high-resolution lateral radiograph; (B) and (C) saggital undecalcified histologic section and corresponding microradiograph. Animal was graded as radiographically fused, and histologic evaluation demonstrated partial fusion. This histologic section shows no bony bridging.

graded as radiographically fused. Histologic sections confirmed solid fusion, with bone growth through the interior of the implant. One of the tantalum markers is visible in histologic section and microradiograph.

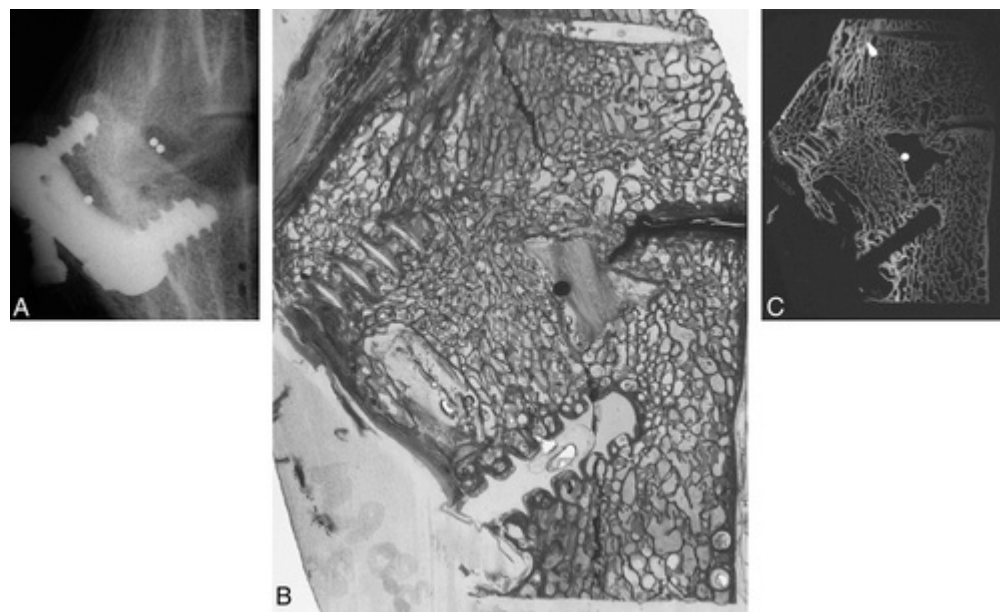


Figure 5. Histologic results at 36 months: (A) postsacrifice high-resolution lateral radiograph; (B) and (C) sagittal undecalcified histologic section and corresponding microradiograph. Animal was graded as radiographically fused. Histologic sections confirmed solid fusion, and complete resorption of the implant. One of the tantalum markers is visible in histologic section and microradiograph.